High Prevalence of SARS-CoV-2 Omicron Infection Despite High Seroprevalence, Sweden, 2022

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We performed 2 surveys during 2022 to estimate point prevalences of SARS-CoV-2 infection compared with overall seroprevalence in Sweden. Point prevalence was 1.4% in March and 1.5% in September. Estimated seroprevalence was >80%, including among unvaccinated children. Continued SARS-CoV-2 surveillance is necessary for detecting emerging, possibly more pathogenic variants.

The SARS-CoV-2 Omicron variant has had strong effects on the COVID-19 pandemic. New Omicron subvariants have emerged over time and those subvariants have increased capacity to evade neutralizing antibody responses induced by both vaccines and prior infections, causing breakthrough infections and reinfections (*1*–*4*). After general PCR testing was halted in Sweden in early 2022, the possibility to track the COVID-19 situation and maintain surveillance in the general population largely depended on point prevalence surveys to detect acute SARS-CoV-2 infection by using PCR and estimates of previous infections by using serology. We performed 2 cross-sectional surveys during 2022 to estimate SARS-CoV-2 point prevalences and overall seroprevalence in Sweden.

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The Study

Participants were invited from a nationwide probability-based web panel (*5*,*6*). Participants received material for sampling and instructions on how to perform self-sampling at home (Appendix, https://wwwnc.cdc.gov/EID/article/29/6/22-1862-App1.pdf). The first survey, March 21–25, covered all 21 regions in Sweden; the second survey, September 26–29, covered 11 regions in the country, representing 64% of the population. We performed surveys as part of the Public Health Agency of Sweden's assignment to monitor communicable diseases and evaluate infection control measures (in accordance with §§18 of Ordinance 2021:248 from the Swedish Parliament). All participants provided informed consent, and the legal guardian provided consent for persons <16 years of age.

In March, 11,334 persons were invited and 2,906 persons 2–96 years of age participated (Appendix Table 1). In total, we analyzed 2,659 samples for ongoing infection and 2,587 samples for serologic responses (Figure, panel A). We detected 48 PCR-positive samples showing SARS-CoV-2 infection, an estimated point prevalence of 1.4% (95% CI 0.9%–2.1%) in the population of Sweden at the end of March. One infection was caused by the Delta variant and 47 by Omicron subvariants (Appendix Table 2). Data from the national registry for communicable diseases revealed that 633 (24%) of the 2,659 participants with a valid PCR result had $\geq$1 previous confirmed SARS-CoV-2 infection; 79.4% had received $\geq$3 vaccine doses (Table 1). Among 48 participants with PCR-positive results, 4 (8.3%) had previously

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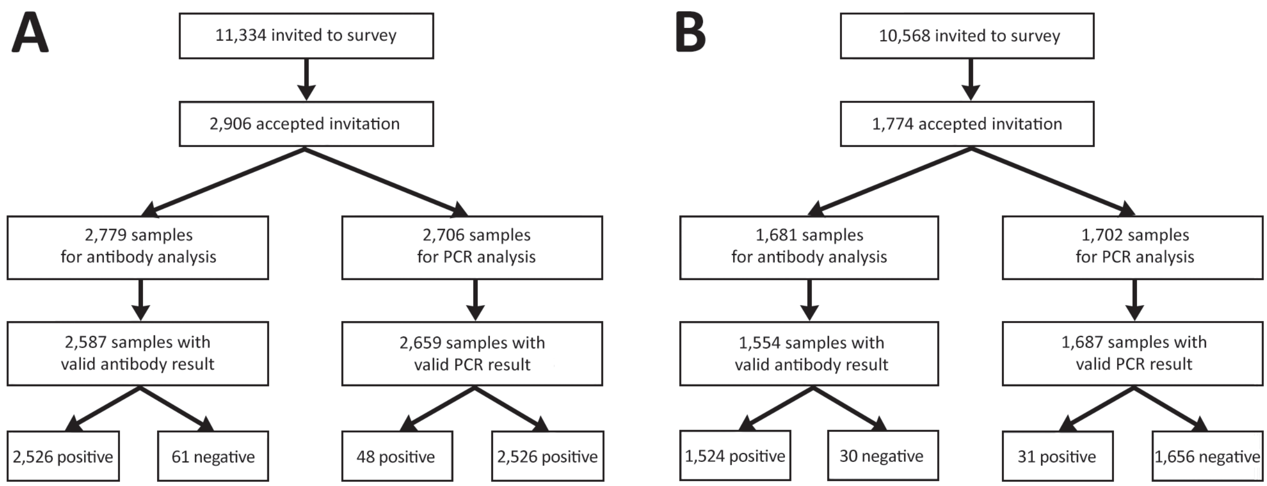

Figure. Flowchart of study participant enrollment and collected and analyzed samples in a study of prevalence of SARS-CoV-2 Omicron infection despite high seroprevalence, Sweden, 2022. A) Surveys performed during March 21–25. B) Surveys performed September 26–29. Point prevalence and Omicron subvariant data from the September study was published previously (*6*).

reported SARS-CoV-2 infections. On the basis of spike IgG data from the 2,587 participants with a valid sample for serology, we estimated a 93.3% (95% CI 91.5%–94.8%) SARS-CoV-2 seroprevalence in the population of Sweden at the end of March 2022. The estimated seroprevalence was 80.1% (95% CI 71.1%–87.4%) in children ≤11 years of age and 94.2%–98.8% in persons >11 years of age (Table 2).

In the September survey, 10,568 persons were invited and 1,774 persons 2–94 years of age participated. We were able to analyze 1,687 samples for ongoing infection (Appendix Table 1), and 1,554 samples for serologic responses (Figure, panel B). We previously reported that 31 of 1,687 participants were PCR-positive in September, that the estimated point prevalence was 1.5% (95% CI 0.9%–2.5%), and all infections were caused by Omicron subvariants (*6*). Among participants in the September survey, 485 (29%) had ≥1 previously confirmed SARS-CoV-2 infection; 85.5% had received ≥3 vaccine doses (Table 1). Among PCR-positive participants, 22 (71%) had previously reported SARS-CoV-2 infections. On the basis of spike IgG data (n = 1,554), we estimated that SARS-CoV-2 seroprevalence in Sweden was 93.1% (95% CI 89.2%–96.0%) at end of September. Estimated seroprevalence was 84.0% (95% CI 70.3%–93.3%) in persons 2–11 years of age and 84.9%–100% in persons >11 years of age (Table 2).

Using answers in the participant symptom survey, we next analyzed for symptoms in general and for symptoms among SARS-CoV-2–infected participants. Overall, 65.2% of participants in March and 67.7% of participants in September, experienced ≥1 symptom within 2 weeks before sampling. Of participants with negative PCR results, 64.6% in March and 67.3% in September had ≥1 symptom (Appendix Table 3). Among 79 PCR-positive participants, 4 had no symptoms within 2 weeks before sampling (Appendix Table 3), and 3 of those 4 experienced symptoms within 1 week after sampling.

Conclusions

Beginning February 9, 2022, mainly hospitalized persons, healthcare workers, long-term care facility staff, and at-risk persons with symptoms indicating COVID-19, were tested for SARS-CoV-2 infection in Sweden. Because the general population was no longer tested, trends in prevalence and transmission patterns were difficult to assess in real-time. To estimate point prevalence of infection in the population, Sweden needed random sampling of the population on a nationwide level.

We estimated point prevalences in Sweden of 1.4% during March 21–25 and, as previously reported (*6*), 1.5% during September 26–29. Those estimated point prevalences were higher than those in our previous national surveys (*5*). In another survey of

Table 1. Number of COVID-19 vaccine doses received by participants in surveys conducted for study of high prevalence of SARS-CoV-2 Omicron infection despite high seroprevalence, Sweden, 2022

No. doses	No. participants (%)	
	March 21–25, n = 2,659	September 26–29, n = 1,687
0	178 (6.9)	96 (6.2)
1	12 (0.5)	5 (0.3)
2	343 (13.3)	126 (8.1)
3	2,006 (77.5)	809 (52.1)
4	48 (1.9)	408 (26.3)
5	0	110 (7.1)

Table 2. Estimated SARS-CoV-2 seroprevalence by age group in study of high prevalence of SARS-CoV-2 Omicron infection despite high seroprevalence, Sweden, 2022

Age group	% Participants (95% CI)	
	March 21–25, n = 2,587	September 26–29, n = 1,554
1–11	80.1 (71.1–87.4)	84.0 (70.3–93.3)
12–19	97.2 (81.9–100.0)	84.9 (53.2–99.0)
20–29	95.9 (89.6–99.2)	92.7 (70.8–100.0)
30–49	94.2 (89.4–97.5)	95.9 (89.7–99.2)
50–64	95.3 (91.6–97.9)	95.0 (88.3–98.7)
65–79	95.0 (94.2–95.7)	96.7 (89.2–100.0)
≥80	98.8 (89.8–100.0)	100 (94.3–100.0)

healthcare workers in Stockholm during June 28–29, 2022, we observed asymptomatic SARS-CoV-2 infections in 2.3% of participants (*7*). Although healthcare workers are likely at higher risk for infection than the general population, those 3 surveys collectively indicated a continued high level of Omicron transmission in Sweden during March, June, and September 2022. Similar, or even higher, point prevalences were reported from other countries during 2022. For example, surveys performed on the general population in the United Kingdom estimated point prevalences of 6.7%–8.7% in March and 2.1%–2.5% in September for England, Scotland, Wales, and Northern Ireland (*8*). Moreover, a survey of blood donors in Denmark estimated that, by March 2022, ≈66% of the age-matched healthy population had been infected by SARS-CoV-2 in <5 months (*9*). Taken together, those and many other reports show the high capacity of Omicron to spread, including among highly vaccinated populations.

A large percentage of the population were positive for spike IgG in March and in September 2022, which can partly be explained by the high vaccine coverage in Sweden. COVID-19 vaccination was not recommended for children <12 years of age in Sweden. Hence, in the youngest, unvaccinated, age group, seroconversion was likely induced solely by infection, indicating that a large percentage (80%) of that age group had already been infected with SARS-CoV-2 by March 2022. Similar levels of infections in children have been reported from Bavaria, Germany, including seroprevalences of 67% for preschool children 1–4 years of age and 84% for school-age children 5–10 years of age in June 2022, largely caused by the Omicron variant (*10*).

Current vaccines seem to provide only limited, short-term, inhibitory effect on Omicron transmissibility (*11*). Of note, our surveys showed that among PCR-positive participants in March, 8.3% had a previously recorded SARS-CoV-2 infection, but in September, those participants increased to 71%, indicating a high level of reinfection caused by then circulating Omicron subvariants, which have shown highly increased capacity to avoid neutralizing antibodies (*12*–*14*).

In summary, we estimate that ≈1 of every 66 persons in Sweden was infected with SARS-CoV-2 by March and September 2022. Although Omicron has a high transmission capacity, current vaccines protect against severe disease, as noted by the low fatality rate observed in Omicron-infected persons in Denmark (*9*). However, because Omicron has the capacity to efficiently transmit despite high vaccine coverage, continued surveillance of the general population for early signs of new, more possibly pathogenic, emerging SARS-COV-2 variants remains crucial.

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About the Author

Dr. Groenheit is a microbiologist at the Public Health Agency of Sweden, Solna, Sweden. Her primary interests include tuberculosis, especially focusing on drug resistance and molecular epidemiology, and SARS-CoV-2 prevalence and seroprevalence.

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Appendix

Methods

Survey Population

This investigation was an observational, cross-sectional study. Individuals were invited to participate based on a nationwide probability-based web panel regularly used for health-related questionnaires at the Public Health Agency of Sweden, including previous point-prevalence studies (*1*,*2*). All participants provided informed consent. For those under 16 years of age, the legal guardian was asked to, and provided, informed consent. Participation could be withdrawn at any time.

The surveys were performed as part of the Public Health Agency of Sweden's assignment to monitor communicable diseases and evaluate infection control measures in accordance with §§18 of the ordinance (2021:248) from the Swedish Parliament.

Self-Sampling

Participants received material for sampling and instructions on how to perform self-sampling at home. Self-sampling kits for PCR-test contained a sterile cotton swab and a test tube containing 0.5 ml 0.9% saline. Participants performed self-sampling using a cotton swab for swabbing of the pharynx followed by swabbing of the outer nostrils using the same swab. Participants then drooled/spat into a cup and swirled the same cotton swab in the saliva before finally moving the swab to the test tube for 30 seconds of swirling. The swab was then removed, and the test tube tightly closed.

Self-sampling kit for blood sampling contained a device for finger picking and paper for collection of blood on a qDBS (Capitainer). The participants were asked to store the samples in a refrigerator until collection for transport to laboratories for further analysis.

PCR and Sequencing

Samples were analyzed for SARS-CoV-2 by using real-time reverse transcription PCR (RT–PCR) assays routinely used to diagnose COVID-19 in Sweden at the National Pandemic Center, Stockholm, Sweden. To verify that a sample was taken correctly in terms of swabbing against mucosal surfaces in the nose or throat, RNase P mRNA was analyzed. Samples negative for RNase P were excluded from analysis. RT-PCR–positive samples were subsequently sequenced at the Public Health Agency of Sweden, Solna, and SARS-CoV-2 variants were identified based on Pangolin version 4.1.3 and pangolin-data version 1.15.1 (*3*,*4*).

Serologic Response

Samples were extracted from the qDBS, as previously described (*5*,*6*), and then analyzed for spike IgG by using an ELISA with a stringent cutoff for positive detection of S-specific IgG set to optical density (OD) 0.7 or higher, as previously described (J.W. Byström et al., unpub. data).

Statistical Analyses

We estimated the proportion of SARS-CoV-2–positive individuals and the proportion with antibodies to SARS-CoV-2 in the Swedish population and in 11 regions in the second study as a weighted proportion. The weights were based on the sampling weights of the participants in the web panel, calibrated with the GREG estimator (*7*) to adjust for nonresponse bias. The auxiliary information used in the calibration consisted of age, gender, geographic region, and vaccination coverage with at least 2 doses by age group, up to 2 weeks before the first sampling date. The seroprevalence estimates were adjusted to take into account the sensitivity (99.2%) and specificity (99.3%) of the test with the Rogan-Gladen formula (*8*). All estimates are reported with their respective 95% CI that were calculated using the modified Clopper-Pearson method (*9*). Analyses were performed in R (https://www.r-project.org) using the "survey" package version 4.1-1.

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Appendix Table 1. Age and sex distribution of participants in the surveys with a positive or negative SARS-CoV-2 PCR test, Sweden 2022*

	March, no.			September, no.		
Age group, y	F	M	Total no. (%)	F	M	Total no. (%)
1–15	96	77	173 (6.5)	53	40	93 (5.5)
16–29	140	52	192 (7.2)	82	20	102 (6.0)
30–59	885	426	1,311 (49.3)	568	260	828 (49.1)
≥60	523	460	983 (37.0)	360	304	664 (39.4)
Total no. (%)	1,644 (61.8)	1,015 (38.2)	2,659 (100)	1,063 (63.0)	624 (37.0)	1,687 (100)

*Surveys conducted during March 21–25 and September 26–29.

Appendix Table 2. Identified SARS-CoV-2 variants among the PCR-positive samples in March (N = 48).

SARS-CoV-2 variant	No. (%)
AY.111	1 (2.1)
BA.1	1 (2.1)
BA.2	33 (68.8)
BA.2.9	13 (27.1)

Appendix Table 3. Distribution of symptoms within 2 weeks before sampling among participants with a positive or negative SARS-CoV-2 PCR-test, Sweden, 2022.

	March		September	
Symptom	% Infected, n = 48	% Not infected, n = 2,602	% Infected, n = 31	% Not infected, n = 1,648
Runny nose	81.3	28.1	67.7	28.3
Cough	75	16.3	71.0	21.2
Headache	66.7	32.5	71.0	36.8
Sore throat	66.7	14.6	58.1	20.3
Huskiness	56.3	8.0	38.7	10.7
Extreme fatigue, exhaustion	54.2	18.6	38.7	22.6
Fever	47.9	5.7	41.9	7.0
Myalgia	35.4	13.2	32.3	15.5
Chills	25	4.1	25.8	5.0
Joint pain	25	12.5	25.8	14.4
Stomach ache	25	14.2	12.9	13.8
Shortness of breath, difficulty breathing	22.9	6.5	12.9	8.7
Ear pain	20.8	4.1	22.6	4.3
Diarrhea	20.8	9.7	19.4	10.1
Eye discharge	18.8	5.3	16.1	5.6
Nausea	16.7	8.7	12.9	9.5
Loss of smell	10.4	3.4	9.7	3.5
Skin rashes†	8.3	4.5	6.5	4.6
Chest pain	6.3	2.7	6.5	2.7
Loss of taste	6.3	2.6	6.5	2.8
Nose bleeds	4.2	5.7	3.2	3.8
Vomiting	0	2.2	9.7	0.9
No symptoms	2.1	35.4	9.7	32.7

*Surveys conducted during March 21–25 (n = 2,650) and September 26–29 (n = 1,679).
†Includes hives, dots, pustules, or blisters.